

Application No. 10/693,025
Docket No. 9394L
Response dated March 23, 2007
Reply to Office Action of October 23, 2006
Customer No. 27752

REMARKS

Claims 1-19 are pending in the present application. Claim 19 has been withdrawn from consideration. Claims 1-18 have been rejected. Claims 1 and 16 have been amended to more particularly describe Applicants' microspheres and to articulate the method of the present invention. Claims 15 and 17-18 have been amended to particularly claim Applicants' microspheres. No new matter has been added.

ART REJECTIONS

REJECTIONS UNDER 35 USC §103

Claims 1-18 have been rejected under 35 USC §103(a) as being unpatentable over Goldberg et al., US Pub 2001/0041335 (hereinafter "Goldberg") and further in view of Mirkin et al., USP 6,582,921 (hereinafter "Mirkin"). For reasons stated in the record, the Office believes it would have been prima facie obvious to have implemented the labeled polynucleotide sequences with receptors of Goldberg with the binding of oligonucleotides attached to microspheres as taught by Mirkin. Applicants respectfully traverse this rejection.

Goldberg discloses methods and compounds for detecting target nucleic acids in a sample. Goldberg fails to teach or suggest Applicants' claimed method, as amended, using a flow cytometer. Additionally, Goldberg fails to teach or suggest the use of a bead/microsphere coupled with a pre-optimized oligonucleotide, as admitted by the Office. Mirkin provides methods for detecting a nucleic acid wherein the nucleic acid is contacted with one or more types of nanoparticles having oligonucleotides attached thereto. Mirkin also fails to teach or suggest Applicants' claimed method, as amended, using a flow cytometer. Thus, the combination of both references, as suggested by the Office, still fails to address the shortcomings necessary to obviate the presently claimed invention. In determining obviousness, "[t]he claimed invention must be considered as a whole, and the question is whether there is something in the prior art as a whole to suggest the desirability, and the obviousness of making the combination." *Lindeman Maschinenfabrick GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1462 (Fed.

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Cir. 1984); *Maize*, 5 USPQ 1788, 1793 (Fed. Cir. 1988). The fact that the references relate to the same area of technology is insufficient. *In re Geiger*, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Applicants respectfully submit that while their technology may relate to the two cited references, the methods of detection and use of such assays are clearly distinct and unobvious.

For example, both references require the use of a solid surface to immobilize and detect the nucleic acid. Goldberg refers to their surface as "Langmuir Blodgett film, glass, germanium, silicon, (poly)tetrafluorethylene, polystyrene, gallium arsenide, gallium phosphide, silicon oxide, silicon nitride, and combinations thereof." (Goldberg, pg. 2, par. 15). Mirkin corresponds by disclosing "suitable substrates" as those that "include transparent solid surfaces, opaque solid surfaces, and conducting solid surfaces. Preferred are transparent substrates such as glass or plastics." (Mirkin, col. 24, lines 57-67). The present invention is advantageous over the prior art in that it does not require the use of a solid substrate for detection. By quantifying the signal via flow cytometry, Applicants are able to utilize a multiplexed assay platform that quantifies up to 100 distinct analytes simultaneously in a single sample. Furthermore, Mirkin fails to teach or suggest an identifiable fluorescent detectable microsphere which is used within the flow cytometer and read by a two laser system. As disclosed by Applicants, the first laser identifies the analyte by exciting the fluorophores within the bead while the second laser measures the amount of target bound to the coupled polynucleotide on the bead. Thus, without the teaching or suggestion of a flow cytometer and further without a fluorescent bead, both Goldberg and Mirkin, separately or combined, fail to meet the threshold for a *prima facie* obviousness rejection. A skilled artisan reading Goldberg and Mirkin would not think to combine the references and develop an assay that utilizes both flow cytometry and a fluorescent particle. With the emphasis of solid substrates in the assays of both references, a skilled artisan would not consider an alternate state of matter by using liquid, in particular, using liquid without an additional solid surface. Additionally, since flow cytometry only utilizes liquid, it would be impossible for Goldberg or Mirkin to work with Applicants' method and vice-versa. More importantly, because flow cytometry was originally developed for the utilization of protein and not oligonucleotides,

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Goldberg or Mirkin would not have thought to employ a flow cytometer as part of the methodology of their invention. Applicants respectfully submit that there must be a reason apparent at the time the invention was made to a person of ordinary skill in the art for applying the teaching at hand, or the use of the teaching as evidence of obviousness will entail prohibited hindsight. *In re Nomiya, Kohisa, and Matsumara*, 509 F.2d 566, 184 USPQ 607 (CCPA 1975). Again, Applicants submit that in determining obviousness, the entirety of a claimed invention, including the combination viewed as a whole, the elements thereof, and the properties and purpose of the invention, must be considered. *See, In re Wright*, 848 F.2d 1216, 6 USPQ2d 1959, 1961, 1962 (Fed. Cir. 1988).

For the foregoing reasons, it is clear that the presently claimed invention, as amended, is not obviated by the cited references and thus, the rejection under 35 USC §103(a) is improper. Applicants respectfully requests reconsideration and withdrawal of the rejection of claims 1-18.

CONCLUSION

In view of the above, Applicants respectfully submit that each of the issues raised by the Office Action has been addressed. Reconsideration and allowance of each of the pending claims is respectfully requested.

Respectfully Submitted,
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By



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